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(taxane or taxol or paclitaxel) same (polymer) same (nanoparticle or nanosphere)	20

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L2: Entry 86 of 142

File: USPT

Jul 17, 2001

DOCUMENT-IDENTIFIER: US 6262107 B1

TITLE: Water soluble paclitaxel prodrugs

Brief Summary Text (11):

The present invention seeks to overcome these and other drawbacks inherent in the prior art by providing compositions comprising a chemotherapeutic and antiangiogenic drug, such as paclitaxel or docetaxel conjugated to a water soluble polymer such as a polyglutamic acid or a polyaspartic acid, for example, or to a water soluble metal chelator. These compositions are shown herein to be surprisingly effective as anti-tumor agents against exemplary tumor models, and are expected to be at least as effective as paclitaxel or docetaxel against any of the diseases or conditions for which taxanes or taxoids are known to be effective. The compositions of the invention provide water soluble taxoids to overcome the drawbacks associated with the insolubility of the drugs themselves, and also provide the advantages of controlled release so that tumors are shown herein to be eradicated in animal models after a single intravenous administration.

Brief Summary Text (21):

The present invention may also be described in certain embodiments as a method of treating cancer in a subject. This method includes obtaining a composition comprising a chemotherapeutic drug such as paclitaxel or docetaxel conjugated to a water soluble polymer or chelator and dispersed in a pharmaceutically acceptable solution and administering the solution to the subject in an amount effective to treat the tumor. Preferred compositions comprise paclitaxel or docetaxel conjugated to a polyglutamic acids or polyaspartic acids and more preferably to poly (1-glutamic acid) or poly 1-aspartic acid). The compositions of the invention are understood to be effective against any type of cancer for which the unconjugated taxoid is shown to be effective and would include, but not be limited to breast cancer, ovarian cancer, malignant melanoma, lung cancer, gastric cancer, colon cancer, head and neck cancer or leukemia.

Detailed Description Text (5):

The paclitaxel may be rendered water-soluble in two ways: by conjugating paclitaxel to water-soluble polymers which serve as drug carriers, and by derivatizing the antitumor drug with water soluble chelating agents. The latter approach also provides an opportunity for labeling with radionuclides (e.g., ¹¹¹In, ⁹⁰Y, ¹⁶⁶Ho, ⁶⁸G, ^{99m}Tc) for nuclear imaging and/or for radiotherapy studies. The structures of paclitaxel, polyethylene glycol-paclitaxel (PEG-paclitaxel), polyglutamic acid-paclitaxel conjugate (PG-paclitaxel) and diethylenetriaminepentaacetic acid-paclitaxel (DTPA-paclitaxel) are shown in FIG. 1.

Detailed Description Text (37):

The present example demonstrates the conjugation of paclitaxel to a water-soluble polymer, poly (1-glutamic acid) (PG). The potential of water-soluble polymers used as drug carriers is well established (Kopecek, 1990; Maeda and Matsumura, 1989). In addition to its ability to solubilize otherwise insoluble drugs, the drug-polymer conjugate also acts as a slow-release depot for controlled drug release.

Detailed Description Text (41):

To a solution of PG (75 mg, repeating unit FW 170, 0.44 mmol) in dry DMF (1.5 mL) was added 20 mg paclitaxel (0.023 mmol, molar ratio PG/paclitaxel=19), 15 mg dicyclohexylcarbodiimide (DCC) (0.073 mmol) and a trace amount of dimethylaminopyridine (DMAP). The reaction was allowed to proceed at room temperature for 4 hrs. Thin layer chromatography (TLC, silica) showed complete conversion of paclitaxel ($R_f=0.55$) to polymer conjugate ($R_f=0$, mobile phase, $\text{CHCl}_3/\text{MeOH}=10:1$). The reaction mixture was poured into chloroform. The resulting precipitate was collected and dried in a vacuum to yield 65 mg polymer-drug conjugate. By changing the weight ratio of paclitaxel to PG in the starting materials, polymeric conjugates of various paclitaxel concentrations can be synthesized.

CLAIMS:

14. A pharmaceutical composition comprising a conjugate of paclitaxel conjugated to a water soluble polymer comprising a polyglutamic acid polymer, wherein said polyglutamic acid polymer has a molecular weight of about 30,000 to about 60,000 daltons, and said conjugate comprises up to 35% by weight of paclitaxel, wherein said conjugate has a higher water solubility than unconjugated paclitaxel and the ability to accumulate in a tumor.

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File: USPT

Nov 21, 2000

US-PAT-NO: 6150398

DOCUMENT-IDENTIFIER: US 6150398 A

TITLE: Methods for the treatment of cancer

DATE-ISSUED: November 21, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Vande Woude; George F.	Berryville	VA		
Schulz; Nicholas	Pittsburgh	PA		
Zhou; Renping	Frederick	MD		
Daar; Ira	Frederick	MD		
Oskarsson; Marianne	Gaitherburg	MD		

US-CL-CURRENT: [514/449](#); [424/649](#), [549/510](#), [549/511](#)

CLAIMS:

We claim:

1. A method of treating cancer by administering to a human paclitaxel and a DNA cross-linking anti-neoplastic agent, wherein said paclitaxel and DNA cross-linking anti-neoplastic agent act synergistically to inhibit cancerous cell growth in said human.
2. The method of claim 1, wherein said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during G.sub.1 or S phase to inhibit cancerous growth.
3. The method of claim 2, wherein said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during S phase to inhibit cancerous growth.
4. The method of claim 1, wherein said DNA cross-linking anti-neoplastic agent is cisplatin.
5. The method of claim 4, wherein said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during G.sub.1 or S phase to inhibit cancerous growth.
6. The method of claim 5, wherein said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during S phase to inhibit cancerous growth.
7. A method of treating cancer by administering to a human paclitaxel and a

DNA cross-linking anti-neoplastic agent, wherein said paclitaxel exerts an effect on a human cell division cycle during M phase to inhibit cancerous growth, said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during G.sub.1 or S phase to inhibit cancerous growth, and said paclitaxel and DNA cross-linking anti-neoplastic agent act synergistically to inhibit cancerous cell growth in said human.

8. The method of claim 7, wherein said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during S phase to inhibit cancerous growth.

9. The method of claim 7, wherein said DNA cross-linking anti-neoplastic agent is cisplatin.

10. The method of claim 9, wherein said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during S phase to inhibit cancerous growth.

11. A method of treating cancer by administering to a human paclitaxel and a DNA cross-linking anti-neoplastic agent,

wherein said paclitaxel and DNA cross-linking anti-neoplastic agent are administered within eight hours of each other and

act synergistically to inhibit cancerous cell growth in said human.

12. The method of claim 11, wherein said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during G.sub.1 or S phase to inhibit cancerous growth.

13. The method of claim 11, wherein said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during S phase to inhibit cancerous growth.

14. The method of claim 11, wherein said DNA cross-linking anti-neoplastic agent is cisplatin.

15. The method of claim 14, wherein said DNA cross-linking anti-neoplastic agent is administered so as to exert an effect on a human cell division cycle during G.sub.1 or S phase to inhibit cancerous growth.

16. The method of claim 15, wherein said DNA cross-linking anti-neoplastic agent is administered so as to exert an effect on a human cell division cycle during S phase to inhibit cancerous growth.

17. A method of treating cancer by administering to a human paclitaxel and a DNA cross-linking anti-neoplastic agent,

wherein said paclitaxel exerts an effect on a human cell division cycle during M phase to inhibit cancerous growth,

said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during G.sub.1 or S phase to inhibit cancerous growth,

said paclitaxel and DNA cross-linking anti-neoplastic agent are administered within eight hours of each other, and

said paclitaxel and DNA cross-linking anti-neoplastic agent act synergistically to inhibit cancerous cell growth in said human.

18. The method of claim 17, wherein said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during S phase to inhibit cancerous growth.

19. The method of claim 17, wherein said DNA cross-linking anti-neoplastic agent is cisplatin.

20. The method of claim 19, wherein said wherein said DNA cross-linking anti-neoplastic agent is administered so as to exert an effect on a human cell division cycle during S phase to inhibit cancerous growth.

21. A method of treating cancer by administering to a human paclitaxel and DNA cross-linking anti-neoplastic agent,

wherein said paclitaxel and DNA cross-linking anti-neoplastic agent are administered within one hour of each other and

act synergistically to inhibit cancerous cell growth in said human.

22. The method of claim 21, wherein said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during G.sub.1 or S phase to inhibit cancerous growth.

23. The method of claim 22, wherein said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during S phase to inhibit cancerous growth.

24. The method of claim 17, wherein said DNA cross-linking anti-neoplastic agent is cisplatin.

25. The method of claim 21, wherein said DNA cross-linking anti-neoplastic agent is administered so as to exert an effect on a human cell division cycle during G.sub.1 or S phase to inhibit cancerous growth.

26. The method of claim 25, wherein said DNA cross-linking anti-neoplastic agent is administered so as to exert an effect on a human cell division cycle during S phase to inhibit cancerous growth.

27. A method of treating cancer by administering to a human paclitaxel and a DNA cross-linking anti-neoplastic agent,

wherein said paclitaxel exerts an effect on a human cell division cycle during M phase to inhibit cancerous growth, said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during G.sub.1 or S phase to inhibit cancerous growth,

said paclitaxel and DNA cross-linking anti-neoplastic agent are administered within one hour of each other, and

said paclitaxel and DNA cross-linking anti-neoplastic agent act synergistically to inhibit cancerous cell growth in said human.

28. The method of claim 27, wherein said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during S phase to inhibit cancerous growth.

29. The method of claim 27, wherein said DNA cross-linking anti-neoplastic agent is cisplatin.

30. The method of claim 29, wherein said DNA cross-linking anti-neoplastic agent is administered so as to exert an effect on a human cell division cycle during S phase to inhibit cancerous growth.

31. A method of treating cancer by administering to a human paclitaxel and a DNA cross-linking anti-neoplastic agent,

wherein said paclitaxel and DNA cross-linking anti-neoplastic agent are administered to said human in such temporal proximity to each other so as to simultaneously achieve levels of said paclitaxel and DNA cross-linking anti-neoplastic agent in said human sufficient to act synergistically to inhibit cancerous cell growth in said human.

32. The method of claim 31, wherein said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during G.sub.1 or S phase to inhibit cancerous growth.

33. The method of claim 32, wherein said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during S phase to inhibit cancerous growth.

34. The method of claim 31, wherein said DNA cross-linking anti-neoplastic agent is cisplatin.

35. The method of claim 34, wherein said DNA cross-linking anti-neoplastic agent is administered so as to exert an effect on a human cell division cycle during G.sub.1 or S phase to inhibit cancerous growth.

36. The method of claim 35, wherein said DNA cross-linking anti-neoplastic agent is administered so as to exert an effect on a human cell division cycle during S phase to inhibit cancerous growth.

37. A method of treating cancer by administering to a human paclitaxel and a DNA cross-linking anti-neoplastic agent in such temporal proximity to each other so as to simultaneously achieve levels of said paclitaxel and DNA cross-linking anti-neoplastic agent in said human sufficient to act synergistically to inhibit cancerous cell growth in said human,

wherein said paclitaxel exerts an effect on a human cell division cycle during M phase to inhibit cancerous growth, and

said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during G.sub.1 or S phase to inhibit cancerous growth.

38. The method of claim 37, wherein said DNA cross-linking anti-neoplastic agent exerts an effect on a human cell division cycle during S phase to inhibit cancerous growth.

39. The method of claim 37, wherein said DNA cross-linking anti-neoplastic agent is cisplatin.

40. The method of claim 39, wherein said DNA cross-linking anti-neoplastic agent is administered so as to exert an effect on a human cell division cycle during S phase to inhibit cancerous growth.

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L2: Entry 104 of 142

File: USPT

Nov 2, 1999

DOCUMENT-IDENTIFIER: US 5977163 A

**** See image for Certificate of Correction ****

TITLE: Water soluble paclitaxel prodrugs

Brief Summary Text (11):

The present invention seeks to overcome these and other drawbacks inherent in the prior art by providing compositions comprising a chemotherapeutic and antiangiogenic drug, such as paclitaxel or docetaxel conjugated to a water soluble polymer such as a polyglutamic acid or a polyaspartic acid, for example, or to a water soluble metal chelator. These compositions are shown herein to be surprisingly effective as anti-tumor agents against exemplary tumor models, and are expected to be at least as effective as paclitaxel or docetaxel against any of the diseases or conditions for which taxanes or taxoids are known to be effective. The compositions of the invention provide water soluble taxoids to overcome the drawbacks associated with the insolubility of the drugs themselves, and also provide the advantages of controlled release so that tumors are shown herein to be eradicated in animal models after a single intravenous administration.

Brief Summary Text (21):

The present invention may also be described in certain embodiments as a method of treating cancer in a subject. This method includes obtaining a composition comprising a chemotherapeutic drug such as paclitaxel or docetaxel conjugated to a water soluble polymer or chelator and dispersed in a pharmaceutically acceptable solution and administering the solution to the subject in an amount effective to treat the tumor. Preferred compositions comprise paclitaxel or docetaxel conjugated to a polyglutamic acids or polyaspartic acids and more preferably to poly (1-glutamic acid) or poly 1-aspartic acid). The compositions of the invention are understood to be effective against any type of cancer for which the unconjugated taxoid is shown to be effective and would include, but not be limited to breast cancer, ovarian cancer, malignant melanoma, lung cancer, gastric cancer, colon cancer, head and neck cancer or leukemia.

Detailed Description Text (5):

The paclitaxel may be rendered water-soluble in two ways: by conjugating paclitaxel to water-soluble polymers which serve as drug carriers, and by derivatizing the antitumor drug with water soluble chelating agents. The latter approach also provides an opportunity for labeling with radionuclides (e.g., .sup.111 In, .sup.90 Y, .sup.166 Ho, .sup.68 Ga, .sup.99m Tc) for nuclear imaging and/or for radiotherapy studies. The structures of paclitaxel, polyethylene glycol-paclitaxel (PEG-paclitaxel), polyglutamic acid-paclitaxel conjugate (PG-paclitaxel) and diethylenetriaminepentaacetic acid-paclitaxel (DTPA-paclitaxel) are shown in FIG. 1.

Detailed Description Text (37):

The present example demonstrates the conjugation of paclitaxel to a water-soluble polymer, poly (1-glutamic acid) (PG). The potential of water-soluble polymers used as drug carriers is well established (Kopecek, 1990; Maeda and Matsumura, 1989). In addition to its ability to solubilize otherwise insoluble drugs, the drug-polymer conjugate also acts as a slow-release depot for controlled drug release.

Detailed Description Text (41):

To a solution of PG (75 mg, repeating unit FW 170, 0.44 mmol) in dry DMF (1.5 mL) was added 20 mg paclitaxel (0.023 mmol, molar ratio PG/paclitaxel=19), 15 mg dicyclohexylcarbodiimide (DCC) (0.073 mmol) and a trace amount of dimethylaminopyridine (DMAP). The reaction was allowed to proceed at room temperature for 4 hrs. Thin layer chromatography (TLC, silica) showed complete conversion of paclitaxel (Rf=0.55) to polymer conjugate (Rf=0, mobile phase, CHCl₃ / MeOH=10:1). The reaction mixture was poured into chloroform. The resulting precipitate was collected and dried in a vacuum to yield 65 mg polymer-drug conjugate. By changing the weight ratio of paclitaxel to PG in the starting materials, polymeric conjugates of various paclitaxel concentrations can be synthesized.

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L2: Entry 110 of 142

File: USPT

Dec 8, 1998

DOCUMENT-IDENTIFIER: US 5846565 A

**** See image for Certificate of Correction ****

TITLE: Controlled local delivery of chemotherapeutic agents for treating solid tumors

Detailed Description Text (56):

Solid paclitaxel, obtained from Napro Biotherapeutics (Boulder, Colo.) or from the National Cancer Institute (Bethesda, Md.), was mixed with poly[bis(p-carboxyphenoxy)propane-sebacic acid] copolymer (PCPP-SA) (20:80) synthesized according to the method of Domb, A. J., and R. Langer (J. Polym. Sci. 25:3373-3386 (1987)), the teachings of which are incorporated herein by reference, to give a mixture containing 0, 20, 30, or 40% paclitaxel by weight. The paclitaxel-polymer mixture was dissolved in methylene chloride (Fluka, Switzerland) to give a 10% solution (w:v). The solvent was evaporated with a nitrogen stream to yield a dry powder. Paclitaxel-polymer discs (10 mg final weight) were prepared by compression molding 11 mg of the paclitaxel-polymer powder with a stainless steel mold (internal diameter, 2.5 mm) under light pressure from a Carver Press at 200 psi. The discs were sterilized under UV light for 45 minutes.

Detailed Description Text (59):

The efficiency of the delivery of paclitaxel incorporated into a biodegradable polymer into the surrounding medium was assessed in vitro as follows.

Detailed Description Text (61):

Protocol. The paclitaxel-loaded polymer discs were placed in a microporous polyethylene specimen capsule (8.times.8 mm internal diameter and height), which was immersed in 7 ml of 0.1M phosphate buffer, pH 7.4. The apparatus was placed in a 37.degree. C. incubator. The releasing medium was replaced at specified times during the 45-day (1000 hour) incubation period, and the recovered solutions were analyzed by scintillation counting and high pressure liquid chromatography (HPLC). HPLC analysis to confirm the release of intact paclitaxel was performed by extracting 2 ml of solution with methylene chloride and evaporating to dryness. The product was then redissolved in methanol and injected onto a C.sub.1a HPLC column (Licosphere-100RP-18, 5 mm; E Merck, Darmstadt, Germany) as part of a Merck Hitachi system composed of a L-4200 UV-Vis Detector, L-6200 intelligent pump, and D-2500 Chromato integrator). The mobile phase consisted of methanol:water (70:30) and detection was at 230 nm. Control solutions containing 100 mM paclitaxel in methanol were used to determine the retention time of paclitaxel under these conditions (6.73 to 9.04 minutes). Radioactive analysis to quantify the amount of paclitaxel release was done by mixing 200 .mu.l of the releasing buffer solution with 4 ml of a scintillation mixture composed of toluene and Lumax (Landgraaf, The Netherlands) scintillation mixture in a 2:1 volume ratio. This solution was counted on a 1211 Rack .beta.-liquid scintillation counter (LKB-Wallac OY, Finland). Each measurement represents the average of 3 independent countings. At the end of the release period, the amount of drug remaining in the disc was quantified by dissolving the polymer remnant in methylene chloride and counting the solution by the above technique. Release was measured over time from discs containing 20, 30, and 40% paclitaxel by weight.

Detailed Description Text (63):

These results show that paclitaxel is released biphasically from the polymer, with an initial burst phase followed by a slower constant release phase. It is likely that the burst phase corresponds to the rapid release of paclitaxel particles embedded within the matrix surface, while the prolonged release represents slower release of paclitaxel from the center of the matrix. The loading of the polymer does not seem to correlate directly with the amount of paclitaxel released during the experimental period. Although the 40% loaded polymer contained twice as much paclitaxel as the 20% loaded disc, the 40% loaded disc only released 1.25 times as much paclitaxel as the 20% loaded disc after 800 hours in a saline bath. If polymer degradation were the sole determining factor of paclitaxel release, then one would expect the loading to correlate directly with total drug released. Since the correlation appears weakened, another factor must be at least partially controlling paclitaxel release from the disc. Most likely, the low aqueous solubility of paclitaxel limits its uptake into media, despite breakdown of the matrix. Alternatively, the hydrophobicity of paclitaxel may inhibit hydrolysis of the polyanhydride matrix. While such interactions do not preclude the clinical use of this formulation, they do make the pharmacokinetics of the preparation more complex and the results less predictable when implanted in vivo as compared with topically applied or systemically administered.

Detailed Description Text (65):

Demonstration of intracerebral paclitaxel delivery from the polymer matrix in vivo.

Detailed Description Text (66):

The efficiency of the delivery of paclitaxel from the polymer matrix into surrounding brain tissue and the concentration of active paclitaxel within the brain, as measured up to one month after surgical implant, were assessed as follows.

Detailed Description Text (70):

Preparation of the paclitaxel loaded polymer. Polymer discs containing labeled paclitaxel were prepared as above, except that a small amount of ^3H -labeled paclitaxel (specific activity, 19.3 Ci/mmol; National Cancer Institute) in toluene was added to the initial solution of polymer and paclitaxel in methylene chloride. The polymer-paclitaxel mixture was then dried in a vacuum desiccator and pressed into discs using a table vise calibrated to form a pellet.

Detailed Description Text (71):

Paclitaxel-polymer implantation. The procedure for polymer implantation in the rat has been described by Tamargo, R. J., et al. (Cancer Res. 53:329-333 (1993)), the teachings of which are incorporated herein by reference. Briefly, the heads of anesthetized rats were shaved and prepared aseptically. The skull was exposed with a midline incision, and a 3-mm burr hole was drilled through the skull 5 mm posterior and 3 mm lateral to the bregma. The dura was incised with a microsurgical knife (Edward Weck and Co., Inc., Research Triangle Park, N.C.), and the polymer disc was inserted into the brain parenchyma. The wound was irrigated and closed with surgical clips (Clay Adams, Parsippany, N.J.).

Detailed Description Text (73):

To convert dpm/mg tissue to paclitaxel concentration, a second experiment was performed. Four rats were given implants of 40% loaded polymer discs with 0.39 $\mu\text{Ci/mg}$. One rat each was sacrificed at 3, 9, 17, and 30 days. The brain was removed and frozen as above. A 2-mm coronal section was taken through the site of the polymer implant. The section was minced and extracted with ethanol. The ethanol fraction was divided in two. The first half was dried in a vacuum desiccator and then resuspended in 100 μl of ethanol. Samples of this solution were spotted on silica thin layer chromatography plates (Sigma, St. Louis, Mo.). A solution of nonradioactive paclitaxel in ethanol was also applied to the plates over the ethanol extract. The plate was developed with methylene chloride:methanol (95:5)

and exposed in an iodine chamber. The R.sub.f value for the paclitaxel was determined and each lane cut into 4 sections: A, origin; B, origin to paclitaxel spot; C, paclitaxel spot; and D, paclitaxel spot to solvent front. The chromatography strips were combined with Atomlight.TM. mixture and counted in a liquid scintillation counter. The distribution of labeled paclitaxel across the chromatography plate allowed determination of signal corresponding to intact drug. To determine the efficiency of extraction, the remaining half of the original extract was combined with mixture and counted, and the residual brain tissue was homogenized and counted as above. The paclitaxel concentration in ng/mg brain tissue was calculated by multiplying the percentage of intact paclitaxel by the dpm/mg brain and dividing by the specific activity of paclitaxel present in the polymer disc.

Detailed Description Text (81):

The amount of toxicity associated with the paclitaxel loaded polymer implant in the brain was determined as follows.

Detailed Description Text (84):

As shown in Table 4, there was no apparent acute clinical toxicity from the implant. All of the rats recovered from the implant surgery and were indistinguishable from controls in terms of motor activity, response to stimulus, and grooming. Two rats later developed ataxia and, subsequently, hemiplegia contralateral to the implant, weight loss, and death. One rat died spontaneously without a prodrome. All of the other rats remained neurologically intact throughout the experiment. Histological examination of brain tissue sections through the paclitaxel-polymer implant site showed scattered foci of karyorrhectic nuclei interspersed with areas of normal brain. In addition, there were scattered cytologically atypical cells with large, hyperchromatic, sometimes bilobed, nuclei. These atypical cells were more numerous around the implant site, but were seen bilaterally. The changes were present to varying degrees in the brains of all rats receiving the paclitaxel-polymer implant, but were absent in rats receiving the blank PCPP-SA disc, indicating that the cytological changes were a result of the paclitaxel exposure. There was no quantitative or qualitative difference in the visible cytological changes occurring in animals with paclitaxel implants either between groups with different paclitaxel concentration implants or between animals that exhibited gross neurobehavioral toxicity and those that did not. The degree of cytological pathology was, therefore, spread evenly among the different paclitaxel-polymer preparations.

Detailed Description Text (85):

A minimal amount of clinical and histological toxicity was associated with the paclitaxel-polymer implant in the rat brain. Three of the 12 rats receiving the implant (20% loaded polymer) without tumor died during the 60-day experimental period, while the other rats tolerated the treatment without any apparent clinical symptoms. Two rats receiving paclitaxel (20 and 30% loaded polymers) after tumor implantation also died without visible tumor, but with the atypia found in all the rats receiving the paclitaxel implant. These atypical changes were consistent with similar cytological alterations produced by a wide variety of chemotherapeutic agents. The symptoms of overt toxicity appeared late in the experiment, 30 days or more after implant, indicating that acute toxicity is not a primary concern. Interestingly, all the rats receiving the paclitaxel implant had cytological abnormalities visible on microscopic examination, and there was no correlation between the degree of atypia and the presence or severity of clinical toxicity. From the pharmacokinetic measurements of intracerebral drug distribution following implantation, it is apparent that these devices produced high drug concentrations distributed throughout the rat brain. These concentrations were maintained intracranially, for at least one month after implant. It is not surprising, therefore, that the brain itself was affected after prolonged exposure to such high paclitaxel concentrations. Nevertheless, several rats from the tumor-polymer studies lived 120 days or more after implantation, and two lived for one year.

Lower doses of paclitaxel could be used in patients, either from a proportionately smaller polymer disc or from a disc with a lower percentage loading of paclitaxel. These doses could be better tolerated for chronic therapy clinically. Other agents administered interstitially to the brain have been reported to show toxicity in animal models without measurable toxicity in clinical trials. Appropriate dosages for treatment of patients can be determined using standard and routine methods.

Detailed Description Text (87):

Demonstration of the efficacy of the paclitaxel loaded polymer implant at extending survival in rats bearing intracranial 9L gliosarcoma.

Detailed Description Text (88):

The efficacy of the paclitaxel loaded polymer implant at extending survival in rats bearing intracranial 9L gliosarcoma was measured as follows.

Detailed Description Text (90):

Protocol for the intracranial efficacy study. Two separate experiments examining the efficacy of the paclitaxel-polymer implant against the intracranial 9L glioma were performed. Based on in vitro clonogenic assays, the 9L glioma appears relatively resistant to paclitaxel compared to human glioma cells. Intracranial tumor implantation in the rat was performed according to the technique described by Tamargo et al. (1993), the teachings of which are incorporated herein. Briefly, a burr hole was drilled in the dura incised as described above. The cortex and white matter were resected with suction until the superior aspect of the brainstem was visualized. The wound was packed with sterile gauze for 10 minutes to control any bleeding. The gauze was then removed, and a 1-mm^{sup}.3 piece of the 9L gliosarcoma was introduced into the cranial defect and placed on the brainstem. The wound was irrigated and closed with wound clips. Surgery to implant the polymer-chemotherapy device was performed five days later. The rats were randomized to one of the treatment or control groups and weighed. The original incision was reopened aseptically and the placement of the tumor was confirmed. A cruciate incision was made in the surface of the tumor and the polymer disc advanced into the tumor. Treatment rats received 10 mg PCPP-SA discs containing 20, 30, or 40% paclitaxel by weight, while control rats received blank 10 mg PCPP-SA discs containing no paclitaxel. Tamargo et al. have demonstrated that there is no survival difference between rats with intracranial 9L gliomas treated with the blank PCPP-SA discs and rats given a "sham" operation without any implant. Any bleeding was allowed to subside spontaneously, and the wound was irrigated with 0.9% saline and closed with surgical staples. The rats were examined twice daily and the time to death recorded. Long term survivors were sacrificed either 120 days (Experiment 1) or 1 year (Experiment 2) after implant. At death, the brain was removed and fixed in formalin. A coronal section was taken through the polymer implant site and stained with hematoxylin and eosin. The section was examined to confirm the presence or absence of tumor growth. Survival was plotted on a Kaplan-Meier survival curve and statistical significance was determined by a nonparametric Kruskal-Wallis analysis of variance followed by a nonparametric studentized Newman-Keuls test for multiple comparisons, as described by Zar, J. M., Biostatistical Analysis, Prentice-Hall, Inc., Englewood Cliffs, N.J. (1984), the teachings of which are incorporated herein by reference.

Detailed Description Text (92):

As shown in Table 5, two separate experiments established that the paclitaxel polymer implant significantly extended survival in rats bearing the intracranial 9L gliosarcoma compared to control animals. Survival was extended from 1.5 to 3.2-fold (P values from <0.05 to <0.001, respectively, nonparametric Newman-Keuls test). Each polymer preparation produced several long term survivors (120 days or longer from tumor implant). The two long term survivors from Experiment 2 were allowed to live for 1 year prior to sacrifice. None of the surviving animals had visible tumor on autopsy either grossly or microscopically in hematoxylin and eosin-stained sections. In contrast, all animals in the control groups died with large

intracranial tumors. There was no significant survival difference among the treatment doses of each experiment ($P > 0.05$, nonparametric Newman-Keuls).

Detailed Description Text (94):

Thus, the paclitaxel-polymer devices extended the median survival of rats bearing intracranial tumors 1.5- to 3.0-fold ($P < 0.05$ to < 0.001) compared to controls.

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Search Results - Record(s) 91 through 120 of 142 returned.

☐ 91. Document ID: US 6150398 A

Using default format because multiple data bases are involved.

L2: Entry 91 of 142

File: USPT

Nov 21, 2000

US-PAT-NO: 6150398

DOCUMENT-IDENTIFIER: US 6150398 A

TITLE: Methods for the treatment of cancer

DATE-ISSUED: November 21, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Vande Woude; George F.	Berryville	VA		
Schulz; Nicholas	Pittsburgh	PA		
Zhou; Renping	Frederick	MD		
Daar; Ira	Frederick	MD		
Oskarsson; Marianne	Gaitherburg	MD		

US-CL-CURRENT: 514/449; 424/649, 549/510, 549/511

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	FIGS	Drawings
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☐ 92. Document ID: US 6136846 A

L2: Entry 92 of 142

File: USPT

Oct 24, 2000

US-PAT-NO: 6136846

DOCUMENT-IDENTIFIER: US 6136846 A

**** See image for Certificate of Correction ****

TITLE: Formulation for paclitaxel

DATE-ISSUED: October 24, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Rubinfeld; Joseph	Danville	CA		
Gore; Ashok Y.	San Ramon	CA		
Joshi; Rajashree	Union City	CA		
Shrotriya; Rajesh	Danville	CA		

US-CL-CURRENT: 514/449

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Figures	Claims	Index	Drawings
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☐ 93. Document ID: US 6127355 A

L2: Entry 93 of 142

File: USPT

Oct 3, 2000

US-PAT-NO: 6127355

DOCUMENT-IDENTIFIER: US 6127355 A

**** See image for Certificate of Correction ****

TITLE: High molecular weight polymer-based prodrugs

DATE-ISSUED: October 3, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Greenwald; Richard B.	Somerset	NJ		
Pendri; Annapurna	Matawan	NJ		
Zhao; Hong	Piscataway	NJ		

US-CL-CURRENT: 514/183; 514/197, 514/199, 514/263.36, 514/274, 514/279, 514/383,
540/304, 540/460, 544/276, 544/310, 544/314, 548/266.6

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Figures	Claims	Index	Drawings
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☐ 94. Document ID: US 6096331 A

L2: Entry 94 of 142

File: USPT

Aug 1, 2000

US-PAT-NO: 6096331

DOCUMENT-IDENTIFIER: US 6096331 A

TITLE: Methods and compositions useful for administration of chemotherapeutic agents

DATE-ISSUED: August 1, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Desai; Neil P.	Los Angeles	CA		
Soon-Shiong; Patrick	Los Angeles	CA		

US-CL-CURRENT: 424/422; 424/426, 424/428, 424/455, 424/489

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Figures	Claims	Index	Drawings
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☐ 95. Document ID: US 6066673 A

L2: Entry 95 of 142

File: USPT

May 23, 2000

US-PAT-NO: 6066673

DOCUMENT-IDENTIFIER: US 6066673 A

**** See image for Certificate of Correction ****

TITLE: Enzyme inhibitors

DATE-ISSUED: May 23, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
McIver; John McMillan	Cincinnati	OH		
Underiner; Todd Laurence	Cincinnati	OH		
Bates; Timothy	Cincinnati	OH		

US-CL-CURRENT: 514/634; 514/844, 514/846, 564/230, 564/238

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Claims	Drawings
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☐ 96. Document ID: US 6048736 A

L2: Entry 96 of 142

File: USPT

Apr 11, 2000

US-PAT-NO: 6048736

DOCUMENT-IDENTIFIER: US 6048736 A

TITLE: Cyclodextrin polymers for carrying and releasing drugs

DATE-ISSUED: April 11, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kosak; Kenneth M.	West Valley City	UT	84120	

US-CL-CURRENT: 436/536; 436/507, 514/58

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Claims	Drawings
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☐ 97. Document ID: US 6048551 A

L2: Entry 97 of 142

File: USPT

Apr 11, 2000

US-PAT-NO: 6048551

DOCUMENT-IDENTIFIER: US 6048551 A

TITLE: Microsphere encapsulation of gene transfer vectors

DATE-ISSUED: April 11, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hilfinger; John M.	Ann Arbor	MI	48104	
Davidson; Beverly L.	Iowa City	IA	52246	
Beer; Steven J.	Iowa City	IA	52246	
Crison; John R.	Ann Arbor	MI	48103	
Amidon; Gordon L.	Ann Arbor	MI	48109	

US-CL-CURRENT: 424/501; 264/4.1, 264/4.3, 264/4.33, 264/4.7, 424/426, 424/502,
428/402.21

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Index	Draw D.
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☐ 98. Document ID: US 6031133 A

L2: Entry 98 of 142

File: USPT

Feb 29, 2000

US-PAT-NO: 6031133

DOCUMENT-IDENTIFIER: US 6031133 A

**** See image for Certificate of Correction ****

TITLE: Synthetic techniques and intermediates for polyhydroxy, dienyl lactones and
mimics thereof

DATE-ISSUED: February 29, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Smith, III; Amos B.	Merion	PA		
Qiu; Yuping	Philadelphia	PA		
Kaufman; Michael	Philadelphia	PA		
Arimoto; Hirokazu	Drexel Hill	PA		
Jones; David R.	Milford	OH		
Kobayashi; Kaoru	Osaka			JP

US-CL-CURRENT: 564/170

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Index	Draw D.
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☐ 99. Document ID: US 6017948 A

L2: Entry 99 of 142

File: USPT

Jan 25, 2000

US-PAT-NO: 6017948

DOCUMENT-IDENTIFIER: US 6017948 A

TITLE: Water-miscible pharmaceutical compositions

DATE-ISSUED: January 25, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Rubinfeld; Joseph	Danville	CA		
Gore; Ashok Y.	San Ramon	CA		
Joshi; Rajashree	Milpitas	CA		
Shrotriya; Rajesh	Danville	CA		

US-CL-CURRENT: 514/449; 514/922, 514/936, 514/937, 514/941, 514/943, 514/970,
514/974

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Index	Drawings
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☐ 100. Document ID: US 6011008 A

L2: Entry 100 of 142

File: USPT

Jan 4, 2000

US-PAT-NO: 6011008

DOCUMENT-IDENTIFIER: US 6011008 A

TITLE: Conjugates of biologically active substances

DATE-ISSUED: January 4, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Domb; Abraham J.	Efrat			IL
Benita; Shimon	Mevasseret Zion			IL
Polacheck; Itzhack	Jerusalem			IL
Linden; Galina	Bat Yam			IL

US-CL-CURRENT: 514/8; 514/25, 530/395, 536/123.1, 536/18.6, 536/6.4

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Index	Drawings
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☐ 101. Document ID: US 5994341 A

L2: Entry 101 of 142

File: USPT

Nov 30, 1999

US-PAT-NO: 5994341

DOCUMENT-IDENTIFIER: US 5994341 A

TITLE: Anti-angiogenic Compositions and methods for the treatment of arthritis

DATE-ISSUED: November 30, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hunter; William L.	Vancouver			CA
Machan; Lindsay S.	Vancouver			CA

Arsenault; A. Larry

Paris

CA

US-CL-CURRENT: 514/449; 514/250, 514/825, 514/886

Full	Title	Citation	Front	Review	Classification	Date	Reference	Examination	Examination	Claims	Index	Drawings
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☐ 102. Document ID: US 5981568 A

L2: Entry 102 of 142

File: USPT

Nov 9, 1999

US-PAT-NO: 5981568

DOCUMENT-IDENTIFIER: US 5981568 A

** See image for Certificate of Correction **

TITLE: Therapeutic inhibitor of vascular smooth muscle cells

DATE-ISSUED: November 9, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kunz; Lawrence L.	Redmond	WA		
Klein; Richard A.	Edmonds	WA		
Reno; John M.	Brier	WA		

US-CL-CURRENT: 514/411; 514/319, 514/324, 514/422, 514/428, 514/499

Full	Title	Citation	Front	Review	Classification	Date	Reference	Examination	Examination	Claims	Index	Drawings
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☐ 103. Document ID: US 5980927 A

L2: Entry 103 of 142

File: USPT

Nov 9, 1999

US-PAT-NO: 5980927

DOCUMENT-IDENTIFIER: US 5980927 A

TITLE: Method and apparatus for administering analgesics, and method for making same device

DATE-ISSUED: November 9, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Nelson; Timothy S.	Elk River	MN		
Bergan; Matthew A.	Brooklyn Park	MN		

US-CL-CURRENT: 424/425; 424/423, 424/424, 424/426, 514/772.3, 604/890.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Examination	Examination	Claims	Index	Drawings
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☐ 104. Document ID: US 5977163 A

L2: Entry 104 of 142

File: USPT

Nov 2, 1999

US-PAT-NO: 5977163

DOCUMENT-IDENTIFIER: US 5977163 A

**** See image for Certificate of Correction ****

TITLE: Water soluble paclitaxel prodrugs

DATE-ISSUED: November 2, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Li; Chun	Missouri City	TX		
Wallace; Sidney	Houston	TX		
Yu; Dong-Fang	Houston	TX		
Yang; David J.	Sugar Land	TX		

US-CL-CURRENT: 514/449; 424/1.65, 424/9.36, 549/510, 549/511

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	RMIC	Drawings
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☐ 105. Document ID: US 5968543 A

L2: Entry 105 of 142

File: USPT

Oct 19, 1999

US-PAT-NO: 5968543

DOCUMENT-IDENTIFIER: US 5968543 A

**** See image for Certificate of Correction ****

TITLE: Polymers with controlled physical state and bioerodibility

DATE-ISSUED: October 19, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Heller; Jorge	Woodside	CA		
Ng; Steven Y.	San Francisco	CA		

US-CL-CURRENT: 424/425; 424/422, 424/426, 424/486, 528/220, 528/271, 528/354,
528/392, 528/403, 528/406, 528/425

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	RMIC	Drawings
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☐ 106. Document ID: US 5965566 A

L2: Entry 106 of 142

File: USPT

Oct 12, 1999

US-PAT-NO: 5965566

DOCUMENT-IDENTIFIER: US 5965566 A

**** See image for Certificate of Correction ****

TITLE: High molecular weight polymer-based prodrugs

DATE-ISSUED: October 12, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Greenwald; Richard B.	Somerset	NJ		
Pendri; Annapurna	Matawan	NJ		
Zhao; Hong	Piscataway	NJ		

US-CL-CURRENT: 514/279; 514/283, 514/449, 546/48, 546/51, 549/510, 549/511

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Revol	Draw D
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☐ 107. Document ID: US 5916596 A

L2: Entry 107 of 142

File: USPT

Jun 29, 1999

US-PAT-NO: 5916596

DOCUMENT-IDENTIFIER: US 5916596 A

TITLE: Protein stabilized pharmacologically active agents, methods for the preparation thereof and methods for the use thereof

DATE-ISSUED: June 29, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Desai; Neil P.	Los Angeles	CA		
Tao; Chunlin	Beverly Hills	CA		
Yang; Andrew	Rosemead	CA		
Louie; Leslie	Montebello	CA		
Zheng; Tianli	Culver City	CA		
Yao; Zhiwen	Culver City	CA		
Soon-Shiong; Patrick	Los Angeles	CA		
Magdassi; Shlomo	Jerusalem			IL

US-CL-CURRENT: 424/489; 424/439, 424/450, 424/451, 424/465

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Revol	Draw D
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☐ 108. Document ID: US 5886026 A

L2: Entry 108 of 142

File: USPT

Mar 23, 1999

US-PAT-NO: 5886026

DOCUMENT-IDENTIFIER: US 5886026 A

TITLE: Anti-angiogenic compositions and methods of use

DATE-ISSUED: March 23, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hunter; William L.	Vancouver			CA
Machan; Lindsay S.	Vancouver			CA
Arsenault; A. Larry	Paris			CA

US-CL-CURRENT: 514/449

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	Publ	Grant
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☐ 109. Document ID: US 5880131 A

L2: Entry 109 of 142

File: USPT

Mar 9, 1999

US-PAT-NO: 5880131

DOCUMENT-IDENTIFIER: US 5880131 A

**** See image for Certificate of Correction ****

TITLE: High molecular weight polymer-based prodrugs

DATE-ISSUED: March 9, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Greenwald; Richard B.	Somerset	NJ		
Pendri; Annapurna	Matawan	NJ		

US-CL-CURRENT: 514/279; 514/283, 514/449, 546/48, 546/51, 549/510, 549/511

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	Publ	Grant
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☐ 110. Document ID: US 5846565 A

L2: Entry 110 of 142

File: USPT

Dec 8, 1998

US-PAT-NO: 5846565

DOCUMENT-IDENTIFIER: US 5846565 A

**** See image for Certificate of Correction ****

TITLE: Controlled local delivery of chemotherapeutic agents for treating solid tumors

DATE-ISSUED: December 8, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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Brem; Henry	Lutherville	MD	
Langer; Robert S.	Newton	MA	
Domb; Abraham J.	Efrat		IL

US-CL-CURRENT: 424/486; 424/422, 424/426

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Revol	Draw D
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☐ 111. Document ID: US 5840900 A

L2: Entry 111 of 142

File: USPT

Nov 24, 1998

US-PAT-NO: 5840900

DOCUMENT-IDENTIFIER: US 5840900 A

TITLE: High molecular weight polymer-based prodrugs

DATE-ISSUED: November 24, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Greenwald; Richard B.	Somerset	NJ		
Pendri; Annapurna	Matawan	NJ		

US-CL-CURRENT: 546/48; 546/51

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Revol	Draw D
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☐ 112. Document ID: US 5840750 A

L2: Entry 112 of 142

File: USPT

Nov 24, 1998

US-PAT-NO: 5840750

DOCUMENT-IDENTIFIER: US 5840750 A

**** See image for Certificate of Correction ****

TITLE: Discodermolide compounds

DATE-ISSUED: November 24, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Longley; Ross E.	Vero Beach	FL		
Gunasekera; Sarath P.	Vero Beach	FL		
Pomponi; Shirley A.	Fort Pierce	FL		

US-CL-CURRENT: 514/459; 549/292

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Revol	Draw D
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☐ 113. Document ID: US 5801191 A

L2: Entry 113 of 142

File: USPT

Sep 1, 1998

US-PAT-NO: 5801191

DOCUMENT-IDENTIFIER: US 5801191 A

TITLE: Taxoids

DATE-ISSUED: September 1, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bressi; Jerome C.	San Diego	CA		
Douglass, III; James G.	San Diego	CA		
Seligson; Allen	Poway	CA		
Sovak; Milos	LaJolla	CA		

US-CL-CURRENT: 514/449; 549/448, 549/510, 549/511

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	RMK	Draw D.
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☐ 114. Document ID: US 5756536 A

L2: Entry 114 of 142

File: USPT

May 26, 1998

US-PAT-NO: 5756536

DOCUMENT-IDENTIFIER: US 5756536 A

TITLE: Microbial transformation of taxol and cephalomannine

DATE-ISSUED: May 26, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Chen; Shieh-Shung Tom	Morganville	NJ		
Chang; Ching-jer	West Lafayette	IN		

US-CL-CURRENT: 514/449; 549/510, 549/511

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	RMK	Draw D.
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☐ 115. Document ID: US 5719265 A

L2: Entry 115 of 142

File: USPT

Feb 17, 1998

US-PAT-NO: 5719265

DOCUMENT-IDENTIFIER: US 5719265 A

** See image for Certificate of Correction **

TITLE: Polymer-bound paclitaxel derivatives

DATE-ISSUED: February 17, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mongelli; Nicola	Milan			IT
Angelucci; Francesco	Milan			IT
Pesenti; Enrico	Cologno Monzese			IT
Suarato; Antonino	Milan			IT
Biasoli; Giovanni	Gavirate			IT

US-CL-CURRENT: 530/329; 424/78.08, 424/78.13

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	FIGS	Drawings
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☐ 116. Document ID: US 5716981 A

L2: Entry 116 of 142

File: USPT

Feb 10, 1998

US-PAT-NO: 5716981

DOCUMENT-IDENTIFIER: US 5716981 A

TITLE: Anti-angiogenic compositions and methods of use

DATE-ISSUED: February 10, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hunter; William L.	Vancouver			CA
Machan; Lindsay S.	Vancouver			CA
Arsenault; A. Larry	Paris			CA

US-CL-CURRENT: 514/449; 128/898, 526/304, 528/421, 604/20, 604/21, 604/269,
604/508, 606/198, 623/1.15

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	FIGS	Drawings
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☐ 117. Document ID: US 5681847 A

L2: Entry 117 of 142

File: USPT

Oct 28, 1997

US-PAT-NO: 5681847

DOCUMENT-IDENTIFIER: US 5681847 A

** See image for Certificate of Correction **

TITLE: Methods of using discodermolide compounds

DATE-ISSUED: October 28, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Longley; Ross E.	Vero Beach	FL		
Gunasekera; Sarath P.	Vero Beach	FL		

US-CL-CURRENT: 514/459; 549/292

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	PubC	Draw D
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☐ 118. Document ID: US 5651986 A

L2: Entry 118 of 142

File: USPT

Jul 29, 1997

US-PAT-NO: 5651986

DOCUMENT-IDENTIFIER: US 5651986 A

TITLE: Controlled local delivery of chemotherapeutic agents for treating solid tumors

DATE-ISSUED: July 29, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brem; Henry	Lutherville	MD		
Langer; Robert S.	Newton	MA		
Domb; Abraham J.	Efrat			IL

US-CL-CURRENT: 424/484; 424/401, 424/426, 424/486, 424/499

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	PubC	Draw D
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☐ 119. Document ID: US 5648506 A

L2: Entry 119 of 142

File: USPT

Jul 15, 1997

US-PAT-NO: 5648506

DOCUMENT-IDENTIFIER: US 5648506 A

TITLE: Water-soluble polymeric carriers for drug delivery

DATE-ISSUED: July 15, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Desai; Neil P.	Los Angeles	CA		
Soon-Shiong; P.	Los Angeles	CA		
Sandford; Paul A.	Los Angeles	CA		

US-CL-CURRENT: 549/510; 549/511

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	INOC	Draw D.
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☐ 120. Document ID: US 5645988 A

L2: Entry 120 of 142

File: USPT

Jul 8, 1997

US-PAT-NO: 5645988

DOCUMENT-IDENTIFIER: US 5645988 A

TITLE: Methods of identifying drugs with selective effects against cancer cells

DATE-ISSUED: July 8, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Vande Woude; George F.	Berryville	VA		
Koo; Han-Mo	Gaithersburg	MD		
Monks; Anne	Clarksburg	MD		

US-CL-CURRENT: 435/6; 435/32

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	INOC	Draw D.
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Terms	Documents
(taxane or taxol or paclitaxel) adj5 polymer	142

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L2: Entry 113 of 142

File: USPT

Sep 1, 1998

DOCUMENT-IDENTIFIER: US 5801191 A

TITLE: Taxoids

Drawing Description Text (19):

Taxoids of the subject invention may be described by the following formula:

##STR1## wherein R.sub.1 and R.sub.2 are one of OH, R.sub.5, or R.sub.6, with the proviso that at least one of R.sub.1 and R.sub.2 is other than OH and when R.sub.6, there is only one R.sub.6 and the paclitaxel is bonded to a unit of a polymer, which polymer is at least about 5kD.

Drawing Description Text (32):

Of particular interest are paclitaxel:polymer conjugate taxoids where the paclitaxel moiety is attached to the polymer through a hydrolyzable linkage. For the most part the hydrolyzable linkages will be ester linkages, particularly where these linkages are in proximity to a carboxy group, usually on a .beta. or .gamma. carbon to the ester linkage, so as to provide for a taxoid with drug release half-life from the polymer of between 4 and 24 hours, and preferably between 5 and 7 hours. Specific polymer:paclitaxel conjugates of interest include methyl vinyl ether/maleic anhydride:paclitaxel conjugate, (BP-172), hydroxyethyl acrylate/acrylamide/maleic anhydride:paclitaxel conjugate, vinyl acetate/maleic anhydride:paclitaxel conjugate, vinyl acetate/acrylic acid:paclitaxel conjugate, and the like.

Detailed Description Text (45):

Methyl vinyl ether/maleic anhydride copolymer (weight average molecular weight=50,000, 30 mg) was dissolved in dry THF (6mL) with heating. After the solution was cooled to room temperature, paclitaxel (60 mg, 0.07 mmol) was added, followed by LiN[Si(CH.sub.3).sub.3].sub.2 (1 M solution in THF, 150 .mu.L, 0.15 mmol) in a single portion. The reaction was allowed to proceed for 1 hour at which point HPLC (size exclusion chromatography) indicated that 70% of the paclitaxel added was bound to the polymer. The solvent was removed on a rotary evaporator and EtOAc (5 mL) was added. The precipitated solid was centrifuged, the supernatant decanted and the process repeated (3 mL EtOAc.times.4). After drying at 65.degree. C. under high vacuum, the solid weighed 72 mg. Size exclusion chromatography showed that the polymer had a purity of 98%, with ca. 1% free paclitaxel present. U.V. analysis for paclitaxel content indicated 56% (w/w) which correlated with the HPLC-derived value. The reaction scheme is provided in FIG. 9.

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L2: Entry 123 of 142

File: USPT

Dec 5, 1995

DOCUMENT-IDENTIFIER: US 5473055 A

TITLE: Polymer-bound paclitaxel derivatives

Brief Summary Text (1):

The present invention is directed to polymer-bound paclitaxel and polymer-bound paclitaxel derivatives endowed with antitumor -activity, to a method for their preparation and to pharmaceutical compositions containing them.

Brief Summary Text (5):

Preferably, the mol % of units containing the paclitaxel and paclitaxel derivatives is from 0.5 to 2, more preferably, the content of paclitaxel in the polymer was from 2 to 10 % (w/w), most preferred compounds are those characterized by a content of from 4 to 7 % (w/w). The wavy line denotes that the oxygen linked at position 7 of the paclitaxel structure may be in both configurations, i.e. .beta. (natural) or .alpha..

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☐ 1. Document ID: US 6830747 B2

Using default format because multiple data bases are involved.

L3: Entry 1 of 20

File: USPT

Dec 14, 2004

US-PAT-NO: 6830747

DOCUMENT-IDENTIFIER: US 6830747 B2

TITLE: Biodegradable copolymers linked to segment with a plurality of functional groups

DATE-ISSUED: December 14, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lang; Meidong	Ann Arbor	MI		
Chu; Chih-Chang	Ithaca	NY		

US-CL-CURRENT: [424/78.17](#); [424/78.18](#), [424/78.19](#), [424/78.21](#), [525/185](#), [525/186](#), [525/188](#), [525/190](#), [525/411](#), [525/412](#), [525/415](#), [525/418](#), [525/450](#), [623/1.42](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	PubC	Drawings
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☐ 2. Document ID: US 6753006 B1

L3: Entry 2 of 20

File: USPT

Jun 22, 2004

US-PAT-NO: 6753006

DOCUMENT-IDENTIFIER: US 6753006 B1

TITLE: Paclitaxel-containing formulations

DATE-ISSUED: June 22, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Desai; Neil P.	Los Angeles	CA		
Soon-Shiong; Patrick	Los Angeles	CA		

US-CL-CURRENT: [424/422](#); [424/400](#), [424/451](#), [424/484](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	PubC	Drawings
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☐ 3. Document ID: US 6641833 B2

L3: Entry 3 of 20

File: USPT

Nov 4, 2003

US-PAT-NO: 6641833

DOCUMENT-IDENTIFIER: US 6641833 B2

TITLE: Methods for treating ovarian cancer, poly (phosphoester) compositions, and biodegradable articles for same

DATE-ISSUED: November 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Dang; Wenbin	Belle Mead	NJ		

US-CL-CURRENT: 424/426; 424/422, 424/423, 424/486, 514/772.3

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	FIGS	Drawings
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☐ 4. Document ID: US 6630156 B1

L3: Entry 4 of 20

File: USPT

Oct 7, 2003

US-PAT-NO: 6630156

DOCUMENT-IDENTIFIER: US 6630156 B1

TITLE: Process for preparing biodegradable microspheres containing physiologically active agents

DATE-ISSUED: October 7, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Seo; Min Hyo	Taejon-si			KR
Lee; Jae Yong	Daejon-si			KR
Kim; Jee Hyang	Daejon-si			KR

US-CL-CURRENT: 424/426; 424/462, 424/493, 424/499

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	FIGS	Drawings
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☐ 5. Document ID: US 6610317 B2

L3: Entry 5 of 20

File: USPT

Aug 26, 2003

US-PAT-NO: 6610317

DOCUMENT-IDENTIFIER: US 6610317 B2

TITLE: Porous paclitaxel matrices and methods of manufacture thereof

DATE-ISSUED: August 26, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Straub; Julie	Winchester	MA		
Bernstein; Howard	Cambridge	MA		
Chickering, III; Donald E.	Framingham	MA		
Khattak; Sarwat	Amherst	MA		
Randall; Greg	Somerville	MA		

US-CL-CURRENT: 424/422; 424/426, 424/489, 514/449

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	RMIC	Drawings
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☐ 6. Document ID: US 6599519 B1

L3: Entry 6 of 20

File: USPT

Jul 29, 2003

US-PAT-NO: 6599519

DOCUMENT-IDENTIFIER: US 6599519 B1

TITLE: Biodegradable poly(alkylene oxide)-poly(p-dioxanone) block copolymer soluble in organic solvents, and drug delivery composition comprising same

DATE-ISSUED: July 29, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Seo; Min-Hyo	Daejeon			KR
Choi; In-Ja	Daejeon			KR

US-CL-CURRENT: 424/426; 424/184.1, 424/400, 424/402, 424/422, 424/423, 424/451, 424/484, 424/486, 424/487, 424/489

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	RMIC	Drawings
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☐ 7. Document ID: US 6589563 B2

L3: Entry 7 of 20

File: USPT

Jul 8, 2003

US-PAT-NO: 6589563

DOCUMENT-IDENTIFIER: US 6589563 B2

** See image for Certificate of Correction **

TITLE: Drug delivery system exhibiting permeability control

DATE-ISSUED: July 8, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Prokop; Ales	Nashville	TN		

US-CL-CURRENT: [424/490](#); [424/489](#), [424/493](#), [424/494](#), [424/496](#), [424/497](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	PubC	Draw D
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☐ 8. Document ID: US 6537585 B1

L3: Entry 8 of 20

File: USPT

Mar 25, 2003

US-PAT-NO: 6537585

DOCUMENT-IDENTIFIER: US 6537585 B1

TITLE: Methods and compositions for treating solid tumors

DATE-ISSUED: March 25, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Dang; Wenbin	Ellicot City	MD		
Garver, Jr.; Robert I.	Hoover	AL		

US-CL-CURRENT: [424/501](#); [424/502](#), [514/772.3](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	PubC	Draw D
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☐ 9. Document ID: US 6506405 B1

L3: Entry 9 of 20

File: USPT

Jan 14, 2003

US-PAT-NO: 6506405

DOCUMENT-IDENTIFIER: US 6506405 B1

** See image for Certificate of Correction **

TITLE: Methods and formulations of cremophor-free taxanes

DATE-ISSUED: January 14, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Desai; Neil P.	Los Angeles	CA		
Soon-Shiong; Patrick	Los Angeles	CA		

US-CL-CURRENT: [424/450](#); [424/422](#), [424/426](#), [424/428](#), [424/455](#), [424/481](#), [424/491](#),
[424/497](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	PubC	Draw D
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☐ 10. Document ID: US 6482439 B2

L3: Entry 10 of 20

File: USPT

Nov 19, 2002

US-PAT-NO: 6482439

DOCUMENT-IDENTIFIER: US 6482439 B2

TITLE: Drug delivery system exhibiting permeability control

DATE-ISSUED: November 19, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Prokop; Ales	Nashville	TN		

US-CL-CURRENT: 424/489; 424/490, 424/497

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	FIGS	Drawings
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☐ 11. Document ID: US 6479067 B2

L3: Entry 11 of 20

File: USPT

Nov 12, 2002

US-PAT-NO: 6479067

DOCUMENT-IDENTIFIER: US 6479067 B2

TITLE: Methods for treating ovarian cancer, poly (phosphoester) compositions, and biodegradable articles for same

DATE-ISSUED: November 12, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Dang; Wenbin	Ellicott City	MD		

US-CL-CURRENT: 424/426; 424/422, 424/423, 424/486, 514/772.3

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	FIGS	Drawings
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☐ 12. Document ID: US 6469132 B1

L3: Entry 12 of 20

File: USPT

Oct 22, 2002

US-PAT-NO: 6469132

DOCUMENT-IDENTIFIER: US 6469132 B1

TITLE: Diblock copolymer and use thereof in a micellar drug delivery system

DATE-ISSUED: October 22, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Eisenberg; Adi	Montreal			CA
Maysinger; Dusica	Montreal			CA
Allen; Christine	Montreal			CA

US-CL-CURRENT: 528/354; 528/355

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	FIGS	Drawings
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☐ 13. Document ID: US 6365191 B1

L3: Entry 13 of 20

File: USPT

Apr 2, 2002

US-PAT-NO: 6365191

DOCUMENT-IDENTIFIER: US 6365191 B1

TITLE: Formulations of paclitaxel, its derivatives or its analogs entrapped into nanoparticles of polymeric micelles, process for preparing same and the use thereof

DATE-ISSUED: April 2, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Burman; Anand C.	Uttar Pradesh			IN
Mukherjee; Rama	Uttar Pradesh			IN
Khattar; Dhiraj	Uttar Pradesh			IN
Kumar; Mukesh	Uttar Pradesh			IN
Bala; Honey	Uttar Pradesh			IN
Shrivastava; Rajiv Kumar	Uttar Pradesh			IN

US-CL-CURRENT: 424/489; 424/450, 424/451, 424/501, 424/78.08, 424/78.17, 514/449

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	FIGS	Drawings
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☐ 14. Document ID: US 6322817 B1

L3: Entry 14 of 20

File: USPT

Nov 27, 2001

US-PAT-NO: 6322817

DOCUMENT-IDENTIFIER: US 6322817 B1

TITLE: Formulations of paclitaxel, its derivatives or its analogs entrapped into nanoparticles of polymeric micelles, process for preparing same and the use thereof

DATE-ISSUED: November 27, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Maitra; Amarnath	Delhi			IN

Sahoo; Sanjeeb Kumar	Delhi	IN
Ghosh; Prasanta Kumar	New Delhi	IN
Burman; Anand C.	Ghaziabad	IN
Mukherjee; Rama	Ghaziabad	IN
Khattar; Dhiraj	Ghaziabad	IN
Kumar; Mukesh	Ghaziabad	IN
Paul; Soumendu	Ghaziabad	IN

US-CL-CURRENT: [424/489](#); [424/486](#), [424/487](#), [424/501](#), [514/772.3](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	RMIC	Trans C.
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☐ 15. Document ID: US 6096331 A

L3: Entry 15 of 20

File: USPT

Aug 1, 2000

US-PAT-NO: 6096331

DOCUMENT-IDENTIFIER: US 6096331 A

TITLE: Methods and compositions useful for administration of chemotherapeutic agents

DATE-ISSUED: August 1, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Desai; Neil P.	Los Angeles	CA		
Soon-Shiong; Patrick	Los Angeles	CA		

US-CL-CURRENT: [424/422](#); [424/426](#), [424/428](#), [424/455](#), [424/489](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	RMIC	Trans C.
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☐ 16. Document ID: US 5766635 A

L3: Entry 16 of 20

File: USPT

Jun 16, 1998

US-PAT-NO: 5766635

DOCUMENT-IDENTIFIER: US 5766635 A

TITLE: Process for preparing nanoparticles

DATE-ISSUED: June 16, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Spenleuhauer; Gilles	Cachan			FR
Bazile; Didier	La Varenne-S.-Hilaire			FR
Veillard; Michel	Sceaux			FR

Prud'Homme; Christian Lyons FR
Michalon; Jean-Paul Lyons FR

US-CL-CURRENT: [424/489](#); [528/491](#), [528/493](#), [977/DIG.1](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	RMK	Draw D.
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☐ 17. Document ID: US 6322817 B1

L3: Entry 17 of 20

File: DWPI

Nov 27, 2001

DERWENT-ACC-NO: 2002-163013

DERWENT-WEEK: 200370

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TITLE: Production of a controlled-release paclitaxel formulation comprises entrapping the drug in polymer nanoparticles prepared from monomer micelles

INVENTOR: BURMAN, A C; GHOSH, P K ; KHATTAR, D ; KUMAR, M ; MAITRA, A ; MUKHERJEE, R ; PAUL, S ; SAHOO, S K

PRIORITY-DATA: 1999IN-DE00263 (February 17, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 6322817 B1	November 27, 2001		010	A61K047/30

INT-CL (IPC): [A61 K 9/14](#); [A61 K 9/50](#); [A61 K 47/30](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	RMK	Draw D.
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☐ 18. Document ID: WO 200121174 A1, AU 200075999 A, EP 1216042 A1

L3: Entry 18 of 20

File: DWPI

Mar 29, 2001

DERWENT-ACC-NO: 2001-299982

DERWENT-WEEK: 200370

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TITLE: Nanoparticle formulation of polymeric micelles comprises physically entrapped paclitaxel or its derivatives or analogs, useful for treating conditions of cell proliferation such as cancer, tumors and rheumatoid arthritis

INVENTOR: BALA, H; BURMAN, A C ; KHATTAR, D ; KUMAR, M ; MUKHERJEE, R ; SHRIVASTAVA, R K

PRIORITY-DATA: 2000IN-DE00641 (July 11, 2000), 1999US-0401927 (September 23, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 200121174 A1	March 29, 2001	E	018	A61K031/337
AU 200075999 A	April 24, 2001		000	A61K031/337
EP 1216042 A1	June 26, 2002	E	000	A61K031/337

INT-CL (IPC): A61 K 9/51; A61 K 31/337; A61 P 35/00

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	EMC	Drawings
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☐ 19. Document ID: MX 2002000381 A1, DE 19932157 A1, WO 200103670 A1, AU 200061574 A, EP 1194123 A2, KR 2002037027 A, CN 1373657 A, JP 2003504323 W, ZA 200200211 A, BR 200013161 A

L3: Entry 19 of 20

File: DWPI

Apr 1, 2003

DERWENT-ACC-NO: 2001-203633

DERWENT-WEEK: 200415

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TITLE: Micro- or nanoparticles production under mild conditions, by high pressure homogenization at low water content and/or low temperature, useful e.g. with drugs or drug-containing polymer matrices

INVENTOR: KRAUSE, K; MAEDER, K ; MUELLER, R H ; MULLER, R H ; MADER, K

PRIORITY-DATA: 1999DE-1032157 (July 13, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
<u>MX 2002000381 A1</u>	April 1, 2003		000	A61K009/14
<u>DE 19932157 A1</u>	January 18, 2001		014	C08J003/02
<u>WO 200103670 A1</u>	January 18, 2001	G	000	A61K009/14
<u>AU 200061574 A</u>	January 30, 2001		000	A61K009/14
<u>EP 1194123 A2</u>	April 10, 2002	G	000	A61K009/14
<u>KR 2002037027 A</u>	May 17, 2002		000	B82B003/00
<u>CN 1373657 A</u>	October 9, 2002		000	A61K009/14
<u>JP 2003504323 W</u>	February 4, 2003		041	A61K009/14
<u>ZA 200200211 A</u>	February 26, 2003		060	A61K000/00
<u>BR 200013161 A</u>	July 22, 2003		000	A61K009/14

INT-CL (IPC): A61 J 3/02; A61 K 0/00; A61 K 7/00; A61 K 9/14; A61 K 9/51; A61 K 31/175; A61 K 31/192; A61 K 31/196; A61 K 31/337; A61 K 31/485; A61 K 31/513; A61 K 31/55; A61 K 31/573; A61 K 38/00; A61 K 47/02; A61 K 47/30; A61 K 47/32; A61 K 47/34; A61 K 47/36; A61 K 47/42; B02 C 19/12; B82 B 3/00; C08 J 3/02; C08 J 3/12

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	EMC	Drawings
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☐ 20. Document ID: CN 1515244 A, WO 9814174 A1, AU 9745929 A, NO 9901620 A, US 5916596 A, EP 961612 A1, CN 1237901 A, AU 718753 B, NZ 335133 A, JP 2001501931 W, BR 9711856 A

L3: Entry 20 of 20

File: DWPI

Jul 28, 2004

DERWENT-ACC-NO: 1998-348021

DERWENT-WEEK: 200469

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TITLE: Delivery of water insoluble bioactive agents as suspended nanoparticles - by

coating agent in organic phase with aqueous protein and/or synthetic polymer as stabiliser, under high shear, notable use for taxol.

INVENTOR: DESAL, N P; LOUIE, L ; MAGDASSI, S ; SOON-SHIONG, P ; TAO, C ; YANG, A ; YAO, Z ; ZHENG, T ; DESAI, N P

PRIORITY-DATA: 1996US-0720756 (October 1, 1996), 1993US-0023698 (February 22, 1993), 1995US-0412726 (March 29, 1995)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
<u>CN 1515244 A</u>	July 28, 2004		000	A61K009/107
<u>WO 9814174 A1</u>	April 9, 1998	E	071	A61K009/14
<u>AU 9745929 A</u>	April 24, 1998		000	
<u>NO 9901620 A</u>	June 1, 1999		000	
<u>US 5916596 A</u>	June 29, 1999		000	
<u>EP 961612 A1</u>	December 8, 1999	E	000	
<u>CN 1237901 A</u>	December 8, 1999		000	
<u>AU 718753 B</u>	April 20, 2000		000	
<u>NZ 335133 A</u>	December 22, 2000		000	
<u>JP 2001501931 W</u>	February 13, 2001		058	A61K047/30
<u>BR 9711856 A</u>	November 6, 2001		000	

INT-CL (IPC): A61 J 3/00; A61 K 9/107; A61 K 9/14; A61 K 9/38; A61 K 31/337; A61 K 45/00; A61 K 47/30; A61 K 47/42; A61 K 47/48; A61 K 49/00; A61 P 29/00; A61 P 35/00

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	PubC	Draw D.
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Terms

(taxane or taxol or paclitaxel) same (polymer) same (nanoparticle or nanosphere)

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L3: Entry 16 of 20

File: USPT

Jun 16, 1998

DOCUMENT-IDENTIFIER: US 5766635 A

TITLE: Process for preparing nanoparticles

Brief Summary Text (29):

The formation of nanoparticles may be performed in the presence of a pharmaceutical active principle, which may be introduced either in the solvent of the copolymer or in the precipitation solvent. Suitable pharmaceutical active principles include spiramycin, taxanes, such as Taxotere.RTM. (docetaxel) and taxol. It will be appreciated by one skilled in the pharmaceutical arts that other active principles may be used in accordance with the present invention. The active principle should preferably be soluble in the solvent of the polymer and insoluble in water. Although it is still possible to form nanoparticles if the active principle is soluble in water, the yield thereof may be reduced.

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